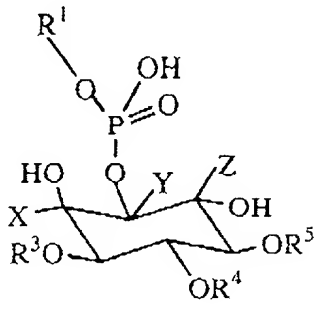
A

EXHIBIT A
PENDING CLAIMS
Divisional Application of 09/292,242 (4020.000500; NUBI:005)

21. A substantially purified sphingo-phosphoinositol analogue of a phosphoinositide compound that comprises at least a first stable or radioactive isotope label within the inositol, ceramide or sphingosine residue of said phosphoinositide compound; wherein said stable or radioactive isotope label is selected from the group consisting of ^{2}H, ^{3}H, ^{32}P, ^{33}P and ^{35}S and wherein said phosphoinositide compound has the *myo*-inositol-based structure:

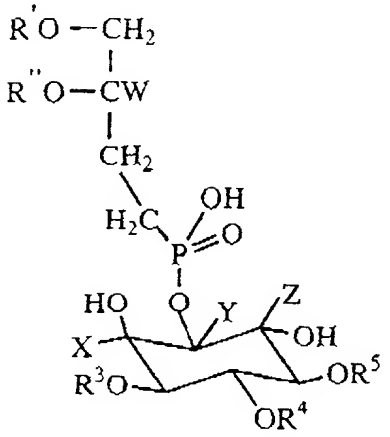


wherein:

R^1 = Ceramide residue or derivative thereof, or Sphingosine residue or derivative thereof;
R^3, R^4, R^5 = H or $Q(T)(OH)_2$;
Q = P, ^{32}P or ^{33}P;
T = O, S or ^{35}S;
W, X, Y, Z = ^{2}H, ^{3}H or H; and

wherein said structure contains at least one ^{2}H, ^{3}H, ^{32}P, ^{33}P or ^{35}S as isotopic label.

22. A substantially purified C-phosphonate analogue of a phosphoinositide compound that comprises at least a first stable or radioactive isotope label within the inositol or the C-phosphonate-phosphatidyl residue of said phosphoinositide compound; wherein said stable or radioactive isotope label is selected from the group consisting of ^{2}H, ^{3}H, ^{32}P, ^{33}P and ^{35}S and wherein said phosphoinositide compound has the *myo*-inositol-based structure:



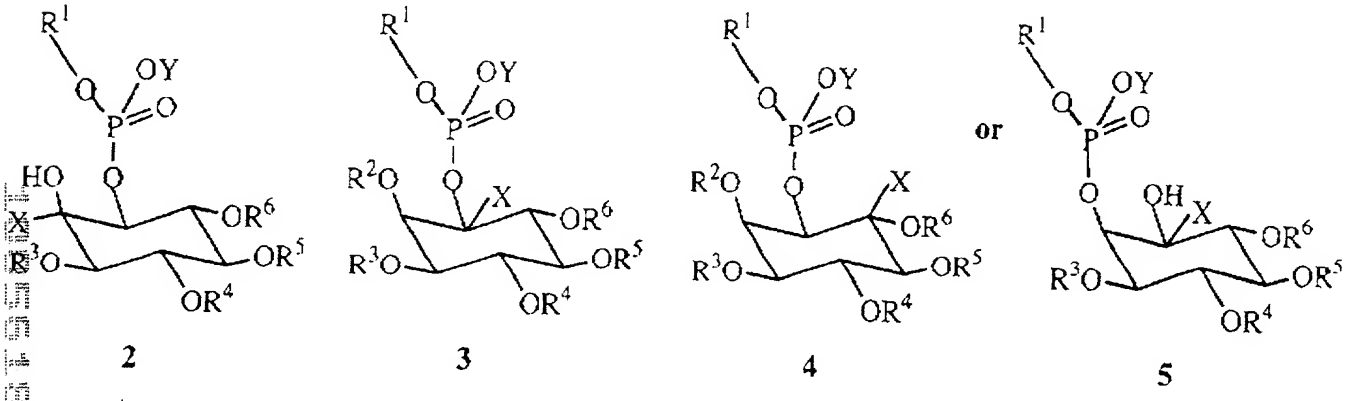
wherein:

R', R'' = fattyacyl, alkyl or H;
R^3, R^4, R^5 = H or $Q(T)(OH)_2$;
Q = P, ^{32}P or ^{33}P;
T = O, S or ^{35}S;
W, X, Y, Z = ^{2}H, ^{3}H or H; and

wherein said structure contains at least one ^{2}H, ^{3}H, ^{32}P, ^{33}P or ^{35}S as isotopic label.

23. The C-phosphonate phosphoinositide compound of claim 22, wherein said phosphoinositide compound comprises at least a first (poly)unsaturated fattyacyl residue.

24. A synthetic intermediate of an isotopically labelled sphingo-phosphoinositol analogue of a phosphoinositide compound, said synthetic intermediate comprising temporary protecting groups at hydroxyl, nitrogen and phosphate positions other than the position into which the isotopic label is to be introduced; wherein said synthetic intermediate has one of the *myo*-inositol-based structures:

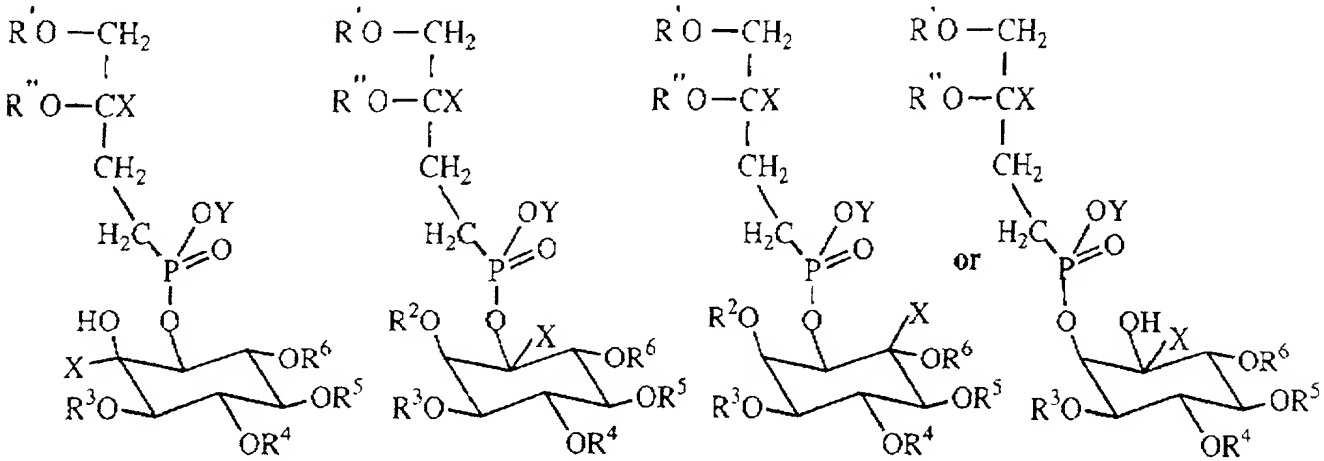


wherein:

X = H, ^{2}H or ^{3}H; Y = alkyl, CH_3, H or (O protecting group);
R^1 = Ceramide residue or derivative thereof, or Sphingosine residue or derivative thereof;
R^3, R^4, R^5 = (OH protecting group), (Q(T)(O protecting group)$_2$), (Q(T)(OH)(O protecting group) or (Q(T)(OH)$_2$);
R^2, R^6 = H or (OH protecting group);
Q = P, ^{32}P or ^{33}P;
T = O, S or ^{35}S; and

wherein said structure contains at least one ^{2}H, ^{3}H, ^{32}P, ^{33}P or ^{35}S as isotopic label.

25. A synthetic intermediate of an isotopically labelled C-phosphonate analogue of a phosphoinositide compound, said synthetic intermediate comprising temporary protecting groups at hydroxyl, phosphonate and phosphate positions other than the position into which the isotopic label is to be introduced; wherein said synthetic intermediate has one of the *myo*-inositol-based structures:



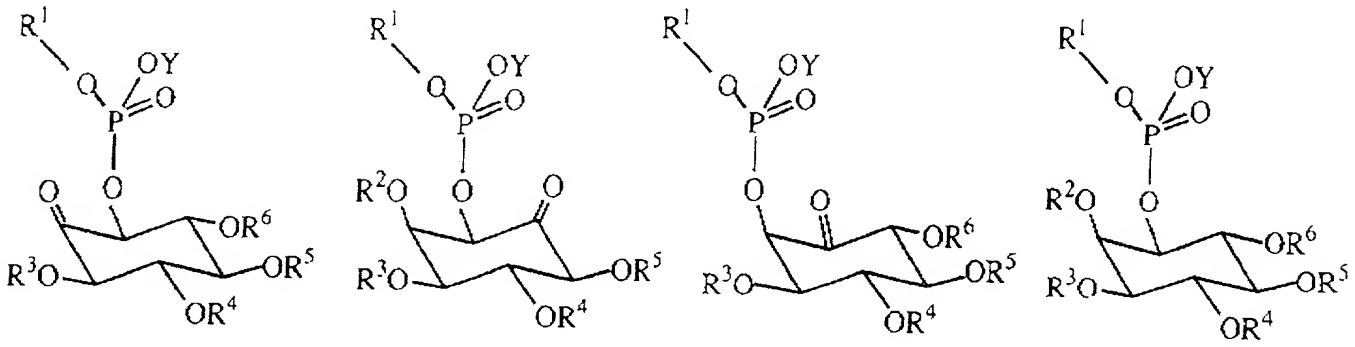
2 3 4 5

wherein:

X = H, ^{2}H or ^{3}H; Y = alkyl, CH_3, H or (O protecting group);
R', R" = fattyacyl, alkyl or H;
R^3, R^4, R^5 = (OH protecting group), (Q(T)(O protecting group)$_2$), (Q(T)(OH)(O protecting group) or (Q(T)(OH)$_2$);
R^2, R^6 = H or (OH protecting group);
Q = P, ^{32}P or ^{33}P;
T = O, S or ^{35}S; and

wherein said structure contains at least one ^{2}H, ^{3}H, ^{32}P, ^{33}P or ^{35}S as isotopic label.

26. A synthetic precursor of a synthetic intermediate of an isotopically labelled sphingo-phosphoinositol analogue of a phosphoinositide compound, wherein said synthetic precursor has a ketone group at the position into which an isotopic ^{2}H or ^{3}H label is to be introduced; wherein said synthetic precursor has one of the structures:



wherein:

Y = alkyl, CH_3 or H;

R^1 = Ceramide residue or derivative thereof, or Sphingosine residue or derivative thereof;

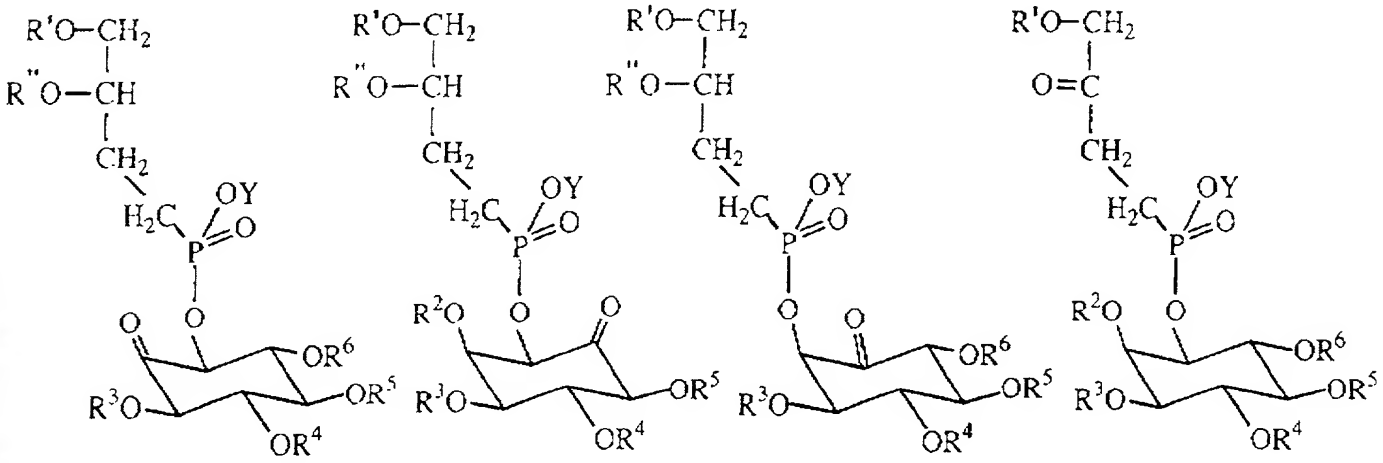
R^3, R^4, R^5 = (OH protecting group), (Q(T)(O protecting group)$_2$), (Q(T)(OH)(O protecting group) or (Q(T)(OH)$_2$);

R^2, R^6 = H or (OH protecting group); and

Q = P, ^{32}P or ^{33}P; and

T = O, S or ^{35}S.

27. A synthetic precursor of a synthetic intermediate of an isotopically labelled C-phosphonate analogue of a phosphoinositide compound, wherein said synthetic precursor has a ketone group at the position into which an isotopic ^{2}H or ^{3}H label is to be introduced; wherein said synthetic precursor has one of the structures:



wherein:

Y = alkyl, CH_3 or H;
R', R" = fattyacyl, alkyl or H;
R^3, R^4, R^5 = (OH protecting group), (Q(T)(O protecting group)$_2$), (Q(T)(OH)(O protecting group) or (Q(T)(OH)$_2$);
R^2, R^6 = H or (OH protecting group); and
Q = P, ^{32}P or ^{33}P; and
T = O, S or ^{35}S.

28. The synthetic intermediate of claim 25, wherein said synthetic intermediate comprises at least a first (poly)unsaturated fattyacyl residue.

29. The synthetic precursor of claim 27, wherein said synthetic precursor comprises at least a first (poly)unsaturated fattyacyl residue.

30. The sphingo-phosphoinositol phosphoinositide compound of claim 21, wherein said phosphoinositide compound further comprises at least a second stable or radioactive isotope label within the ceramide or sphingosine residues of said sphingo-phosphoinositol phosphoinositide compound.

31. The C-phosphonate phosphoinositide compound of claim 22, wherein said phosphoinositide compound further comprises at least a second stable or radioactive isotope label within the alkyl or fattyacyl residues of said C-phosphonate phosphoinositide compound.

32. The sphingo-phosphoinositol phosphoinositide compound of claim 21, wherein said phosphoinositide compound has a structure based on 1D-*myo*-inositol.

33. The sphingo-phosphoinositol phosphoinositide compound of claim 21, wherein said phosphoinositide compound has a structure based on 1L-*myo*-inositol.

34. The C-phosphonate phosphoinositide compound of claim 22, wherein said phosphoinositide compound has a structure based on 1D-*myo*-inositol.

35. The C-phosphonate phosphoinositide compound of claim 22, wherein said phosphoinositide compound has a structure based on 1L-*myo*-inositol.

36. The synthetic intermediate of claim 24, wherein said synthetic intermediate has a structure based on 1D-*myo*-inositol.

37. The synthetic intermediate of claim 24, wherein said synthetic intermediate has a structure based on 1L-*myo*-inositol.

38. The synthetic intermediate of claim 25, wherein said synthetic intermediate has a structure based on 1D-*myo*-inositol.

39. The synthetic intermediate of claim 25, wherein said synthetic intermediate has a structure based on 1L-*myo*-inositol.

40. The synthetic precursor of claim 26, wherein said synthetic precursor has a structure based on 1D-*myo*-inositol.

41. The synthetic precursor of claim 26, wherein said synthetic precursor has a structure based on 1L-*myo*-inositol.

42. The synthetic precursor of claim 27, wherein said synthetic precursor has a structure based on 1D-*myo*-inositol.

43. The synthetic precursor of claim 27, wherein said synthetic precursor has a structure based on 1L-*myo*-inositol.

44. The C-phosphonate phosphoinositide compound of claim 22, wherein said phosphoinositide compound has a structure based on *sn*-glycero-3-phospho as glycerol residue.

45. The C-phosphonate phosphoinositide compound of claim 22, wherein said phosphoinositide compound has a structure based on *sn*-glycero-1-phospho as glycerol residue.

46. The C-phosphonate phosphoinositide compound of claim 22, wherein said phosphoinositide compound has a structure based on *rac*-glycero-3-phospho as glycerol residue.

47. The synthetic intermediate of claim 25, wherein said synthetic intermediate has a structure based on *sn*-glycero-3-phospho as glycerol residue.

48. The synthetic intermediate of claim 25, wherein said synthetic intermediate has a structure based on *sn*-glycero-1-phospho as glycerol residue.

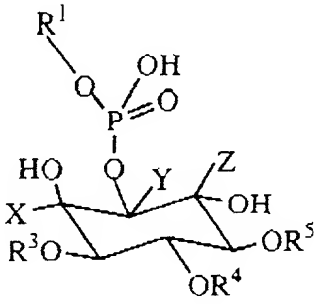
49. The synthetic intermediate of claim 25, wherein said synthetic intermediate has a structure based on *rac*-glycero-3-phospho as glycerol residue.

50. The synthetic precursor of claim 27, wherein said synthetic precursor has a structure based on *sn*-glycero-3-phospho as glycerol residue.

51. The synthetic precursor of claim 27, wherein said synthetic precursor has a structure based on *sn*-glycero-1-phospho as glycerol residue.

52. The synthetic precursor of claim 27, wherein said synthetic precursor has a structure based on *rac*-glycero-3-phospho as glycerol residue.

53. A substantially purified sphingo-phosphoinositol phosphoinositide compound that comprises at least a first stable or radioactive isotope label within the inositol, ceramide or sphingosine residue of said phosphoinositide compound; wherein said stable or radioactive isotope label is selected from the group consisting of ^{2}H, ^{3}H, ^{32}P, ^{33}P and ^{35}S; wherein said phosphoinositide compound has the *myo*-inositol-based structure:

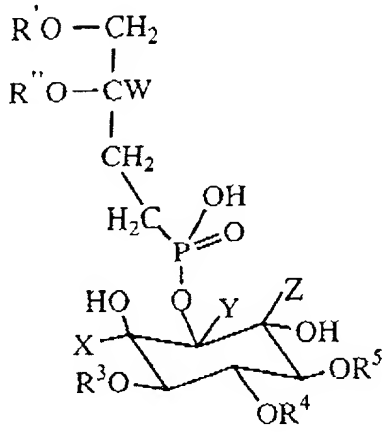


wherein:

R^1 = Ceramide residue or derivative thereof, or Sphingosine residue or derivative thereof;
R^3, R^4, R^5 = H or $Q(T)(OH)_2$;
Q = P, ^{32}P or ^{33}P;
T = O, S or ^{35}S;
W, X, Y, Z = ^{2}H, ^{3}H or H; and

wherein said structure contains at least one ^{2}H, ^{3}H, ^{32}P, ^{33}P or ^{35}S as isotopic label and further comprises temporary protecting groups at hydroxyl and phosphate positions other than the position of at least a first stable or radioactive ^{2}H and ^{3}H isotope label.

54. A substantially purified C-phosphonate phosphoinositide compound that comprises at least a first stable or radioactive isotope label within the inositol or glycerol residue of said phosphoinositide compound; wherein said stable or radioactive isotope label is selected from the group consisting of ^{2}H, ^{3}H, ^{32}P, ^{33}P and ^{35}S; wherein said phosphoinositide compound has the *myo*-inositol-based structure:



wherein:

R', R" = fattyacyl, alkyl or H;
R^3, R^4, R^5 = H or $Q(T)(OH)_2$;
Q = P, ^{32}P or ^{33}P;
T = O, S or ^{35}S;
W, X, Y, Z = ^{2}H, ^{3}H or H; and

wherein said structure contains at least one ^{2}H, ^{3}H, ^{32}P, ^{33}P or ^{35}S as isotopic label and further comprises temporary protecting groups at hydroxyl and phosphate positions other than the position of at least a first stable or radioactive ^{2}H and ^{3}H isotope label.

B

EXHIBIT B
EXPLANATION OF AMENDMENTS
WITH REFERENCE TO SERIAL NO. 09/292,242

The following explanations of the changes in the substitute specification are made with reference to the text of Application Serial No. 09/292,242 as originally filed.

At page 2, lines 3-4 of the text, the deleted text reads "claims priority to co-pending U.S. provisional application Serial No. 60/081,847, filed April 15, 1998. The entire text and figures of this disclosure is" and the inserted text reads --is a continuation of co-pending U.S. application Serial No. 09/292,242, filed April 15, 1999, which claims priority to U.S. provisional application Serial No. 60/081,847, filed April 15, 1998. The entire text and figures of these disclosures are--.

At page 4, lines 2 and 18 of the text, each instance of the deleted text reads "labelling" and each instance of the inserted text reads --labeling--.

At page 6, line 21 of the text, the deleted text reads "*sn*-glcero" and the inserted text reads --*sn*-glycero--.

At page 12, lines 19, 21 and 28 of the text, each instance of the deleted text reads "labelling" and each instance of the inserted text reads --labeling--.

At page 13, line 28 of the text, the deleted text reads "1-phoshphatidyl" and the inserted text reads --1-phosphatidyl--.

At page 13, line 29 of the text, the deleted text reads "labelling" and the inserted text reads --labeling--.

At page 14, line 30 of the text, the deleted text reads "Bu_4NHSO_3," and the inserted text reads -- Bu_4NHSO_4,--.

At page 16, line 23 of the text, the deleted text reads "2-phosphatidyl-1-OH" and the inserted text reads --1-phosphatidyl-1-OH--.

At page 17, line 12 of the text, the deleted text reads "labelling" and the inserted text reads --labeling--.

At page 19, line 29 of the text, the deleted text reads "labelling" and the inserted text reads --labeling--.

At page 24, line 14 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 24, line 15 of the text, the deleted text reads "bisphosphate (DPPtdIns-4,5-P_2)" and the inserted text reads --bis(dibenzylphosphate)--.

At page 25, line 1 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 25, line 2 of the text, the deleted text reads "bisphosphate" and the inserted text reads -- bis(dibenzylphosphate)--.

At page 25, line 4 of the text, the deleted text reads "intermediate" and the inserted text reads -- intermediates--.

At page 25, line 4 of the text, the deleted text reads "labelling" and the inserted text reads --labeling--.

At page 26, line 28 of the text, the deleted text reads "Experiemnts" and the inserted text reads -- Experiments--.

At page 27, line 3, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 27, line 5, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 27, line 9 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 27, line 12 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 27, line 14 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 27, line 16 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 27, line 26 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 27, line 28 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 28, line 2 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 28, line 6 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 28, line 8 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 28, line 11 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 28, line 14 of the text, insert after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 28, line 16 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 28, line 18 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 28, line 22 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 28, line 24 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 28, line 26 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 29, line 2 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 29, line 3 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 29, line 4 of the text, the deleted text reads "genral" and the inserted text reads --general--.

At page 29, line 4 of the text, between "product" and "identical", the inserted text reads --**8a** (X=H)--.

At page 29, line 5 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 29, line 9 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 29, line 11 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 29, line 15 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 29, line 18 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 29, line 19 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 29, line 21 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 29, line 23 of the text, the deleted text reads "the" and the inserted text reads --a--.

At page 29, line 26 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 29, line 28 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 30, line 1 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.

At page 30, line 5 of the text, after "- phospho)" the inserted text reads -- -3,6-di-*O*-benzyl--.